

Do guidelines for the prevention and control of methicillin-resistant *Staphylococcus aureus* make a difference?

H. Humphreys

Department of Clinical Microbiology, The Royal College of Surgeons in Ireland and Beaumont Hospital, Dublin, Ireland

Abstract

Many countries have national guidelines for the prevention and control of methicillin-resistant *Staphylococcus aureus* (MRSA) that are similar in approach. The evidence base for many recommendations is variable, and often, in the drafting of such guidelines, the evidence is either not analysed or not specifically reviewed. Guidelines usually recommend screening and early detection, hand hygiene, patient isolation or cohorting, and decolonization. Although many components of a prevention and control programme appear to be self-evident, e.g. patient isolation, the scientific base underpinning these is poor, and scientifically rigorous studies are required. Nonetheless, where measures, based on what evidence there is and on common sense, are implemented, and where the necessary resources are provided, MRSA can be controlled. In The Netherlands and in other low-prevalence countries, these measures have largely kept health-care facilities MRSA-free. In MRSA-endemic countries, such as Spain and Ireland, national guidelines are often not fully implemented, owing to apparently inadequate resources or a lack of will. However, recent studies from France and Australia demonstrate what is possible in high-prevalence countries when best practice is effectively implemented, with potentially major benefits for patients, the respective health services, and society.

Keywords: Guidelines, isolation/cohorting, methicillin-resistant *Staphylococcus aureus*, review, screening

Clin Microbiol Infect 2009; **15** (Suppl. 7): 39–43

Corresponding author and reprint requests: H. Humphreys, Department of Clinical Microbiology, Education and Research Centre, Royal College of Surgeons in Ireland, Beaumont Hospital, PO Box 9063, Dublin 9, Ireland
E-mail: h Humphreys@rcsi.ie

Background

Methicillin-resistant *Staphylococcus aureus* (MRSA) is a well-recognized cause of healthcare-associated infection (HCAI), and is now increasingly seen outside acute healthcare facilities in some countries. Its clinical impact, in terms of morbidity and mortality, is well recognized. In an observational study of 198 intensive-care units (ICUs) in 24 European countries, *S. aureus* was the most common pathogen implicated in sepsis, and 14% of isolates were MRSA [1]. MRSA bloodstream infection is associated with significant mortality. In a meta-analysis of studies of bloodstream infection due to MRSA and methicillin-susceptible *S. aureus*, there was a significant association between death and MRSA [2].

Given the prevalence of MRSA in many European countries, its clinical impact, and the concern of patients, the public and many healthcare workers, there is widespread

recognition of the need for a multidisciplinary approach to prevention and control. However, the prevalence of MRSA varies considerably among European countries, and from a review of national guidelines, there are some variations in the strategies adopted and in the effectiveness of their implementation.

Guidelines and Recommendations

Although many institutions and professional groups have attempted to address the spread and control of MRSA, the implementation of evidence-based guidelines has been somewhat *ad hoc*. For example, the European Practice Database has collected data on renal practice in different European countries, and found that 1.3% of haemodialysis patients are MRSA-positive [3]. However, in Greece, Italy, England and Belgium, over 50% of centres screen for MRSA, as compared with <10% of centres in Slovakia, Norway, the Czech Republic and Scotland [3].

Guidelines from Germany, New Zealand, North America, The Netherlands, Ireland and the UK have recently been reviewed [4]. Although many of these guidelines share common themes, e.g. the importance of early identification of

MRSA, patient isolation or cohorting, and hand hygiene, the processes by which these guidelines were developed vary somewhat in terms of the analysis of the evidence base. In addition, given the apparent similarity of many aspects of the approach among the various countries, it is somewhat surprising that there is such a range of prevalence among countries, e.g. The Netherlands (low prevalence) and Spain and Ireland (high prevalence). When the literature on interventions to control and prevent MRSA is reviewed, there is often an absence of detail about the infrastructure in which outbreaks or studies occur, and the degree to which there is full support from local organizational and national agencies [5]. A recent assessment of antimicrobial drug use and infection control practices in European hospitals confirms this, as it showed that there were higher levels of MRSA where there were problems in implementing isolation policies, and that lower rates of MRSA were associated with the use of alcohol-based hand hygiene [6].

The Evidence Base for MRSA Guidelines

Much of what is included in local or national recommendations for the prevention and control of MRSA is both logical and self-evident, and the effectiveness of these interventions, when implemented, can be seen in those countries where the prevalence of MRSA infection is low, such as The Netherlands. Nonetheless, it is often difficult to determine from the literature the degree to which individual specific components of a strategy are effective, and where the emphasis is best placed.

In a systematic review of the published literature between 1996 and 2004, well-conducted evaluations reporting the economic benefits arising from infection prevention and control interventions on MRSA were lacking, and for four of five specific interventions, i.e. screening patients before or on admission, the use of surveillance data, isolation/cohorting, and decolonization, the conclusions were at best tentative and far from conclusive, not withstanding the logic associated with each of them [7].

Patient isolation is considered to be one of the most important interventions in reducing the transmissibility of healthcare associated infection. However, a recent review of 46 studies indicated that there were major methodological weaknesses and inadequate reporting in much of the published research [8]. There is a need for greater rigour in the quality of publications that deal with the control and prevention of HCAI. Recently, a set of standards or guidelines has been published to enable researchers and others in the field to check the validity of their studies and results against a

check-list [9]. This approach should promote better studies and enable us to have more valid scientific evidence for much of what is currently practised and implemented in the control and prevention of MRSA.

Current Practice

Although national and local guidelines are often disseminated, it is essential to ascertain whether guidelines are partially or fully implemented when trying to understand prevalence data. In a survey of 36 UK adult cardiac surgical units during 2001, it was found that only 65% of units screened all patients for MRSA, and 45% regularly screened long-term patients remaining in the unit [10], even though the national guidelines at the time identified cardiothoracic units as being high-risk areas for MRSA and recommended admission screening [11]. The authors concluded that there was wide variation in practice within the UK for cardiac surgical units, but that there needed to be some rationalization of preoperative screening and the use of prophylactic antibiotics [10]. In Ireland, a follow-up review of the implementation of recent national guidelines found that 43 of 49 acute hospitals experienced barriers to their full implementation, and in four hospitals there was no education programme on hand hygiene [12].

A multidisciplinary approach that included education, improved ward and theatre hygiene, preadmission, admission and weekly MRSA screening, isolation, and decolonization, largely based on national guidelines [11], resulted in a significant decrease in both the unit acquisition of MRSA and bloodstream MRSA infections, in a London cardiothoracic unit [13]. Also, in a survey of 207 general ICUs in the UK, there was marked variation in practice, including the findings that 75% of units screened patients on admission, isolation cubicles were not present in 10% of units, and 24% of units did not routinely isolate patients with MRSA [14]. These results suggest that up to now, in the UK, national guidelines could not be or were not being implemented. Although a recent UK study has suggested that isolation in the ICU may not be as effective as originally thought [15], there were confounding variables in that study that would have offset the effectiveness of isolation, e.g. suboptimal hand hygiene and admission screening for MRSA, many of which were discussed in the accompanying editorial [16].

In The Netherlands, there is an impressively low prevalence of MRSA in hospitals. In a Dutch study that assessed the prevalence of MRSA among patients without risk factors for MRSA carriage at the time of admission to

hospital, only three MRSA carriers were identified, representing 0.3% of the survey population [17]. When outbreaks of MRSA do occur in The Netherlands, it is clear that considerable efforts are made, with the accompanying resources, to ensure not only that any initial MRSA spread is controlled, but also that MRSA is eradicated, illustrating the effectiveness of the 'search and destroy' approach in low-prevalence countries.

During a recent outbreak in a 700-bed Dutch hospital, additional laboratory resources were provided, the aggressive screening of patient and staff contacts was undertaken, and additional infection prevention and control staff were made available, to assist in outbreak management [18]. Therefore, although this represented an epidemic in a country with low MRSA prevalence rates, as compared with endemic MRSA in many other European countries, best practice consistent with national guidelines ([http://www.wip.nl/UK/free_content/Richtlijnen/MRSA\(1\).pdf](http://www.wip.nl/UK/free_content/Richtlijnen/MRSA(1).pdf)) was implemented and the necessary resources, including finance, space and personnel, were provided. This consistent and comprehensive approach ensured that the outbreak was brought to an end.

Although there are considerable costs associated with such aggressive measures, they appear to be cost-effective. Over a 10-year period (1991–2000), the aggressive implementation of MRSA control measures in The Netherlands resulted in 2265 lost hospitalization days, but this 'search and destroy' approach resulted in the probable prevention of 520 000 infections per year, and the cost of the policy was €280 000 per year [19].

France has had a relatively high national prevalence of MRSA, but efforts have been underway nationally and locally in recent years to improve this situation, with encouraging results. In a programme that involved three ICUs over 7 years, and that consisted in screening and contact precautions, but not routine MRSA decolonization, there was a reduction in MRSA acquired in the ICU from 7% to 2.8% [20]. Similarly, in Australia, a series of interventions in a 35-bed ICU resulted in a decline in the number of MRSA cases in the ICU as well as throughout the hospital [21]. Finally, in the USA, screening policies for MRSA vary among ICUs. However, two recent surveys have highlighted the importance of routine ICU surveillance in establishing the true prevalence of MRSA (both colonization and infection), and the fact that this is an important component in reducing MRSA rates, including MRSA bloodstream infection [22,23]. Therefore, the implementation of recommended measures, whether they be enhanced screening for MRSA, improved hand hygiene, or isolation/cohorting, is effective in reducing rates or minimizing transmission.

Recent and Future Developments

The finding that, in general, national guidelines are not dissimilar in terms of their strategic approach to the prevention and control of MRSA suggests that the differences among countries relates partly to the resources provided for HCAI prevention and control, as well as the priority that is given to such measures, i.e. the culture of the healthcare environment. Although there are some indications that in previously high-prevalence European countries, such as France and Slovenia, improvements have been made (http://www.rivm.nl/earss/Images/EARSS%202006%20Def_tcm61-44176.pdf), there is often discussion in low-prevalence countries of the need to continue to implement aggressive control measures, as these are perceived as being quite costly. A recent review of current policy in The Netherlands in 2006, which was requested by the Dutch Department of Health, concluded that the current, aggressive 'search and destroy' approach should be continued because it results in significantly fewer infections and reduced antibiotic costs (<http://www.gr.nl/pdf.php?ID=1461&p=1>).

Guidelines need to be tailored to the specific clinical circumstances, without compromising the essential principles underpinning them, but there needs to be acceptance from the relevant healthcare professionals. In Canada, a working group has provided clear and sensible advice for the specific management of outbreaks of MRSA in neonatal ICUs [24]. This needs to be accompanied by greater consistency in approach, as suggested by another recent Canadian survey. Although 96% of hospitals screened for MRSA, only 21% conducted regular prevalence surveys, 82% undertook decolonization, and 75% had restrictive antibiotic prescribing [25]. In addition, many countries have recognized the need for guidelines on MRSA in the community to reflect the emergence of true community-acquired strains and the phenomenon of MRSA in healthcare facilities, such as acute hospitals, 'spilling over' into community units and primary care [26].

In the future there may be greater consistency in policies both among institutions and among countries, with greater commitment to their implementation on the part of national and other bodies, driven by patient expectations and demands. However, this will require appropriate governance structures to ensure that a multidisciplinary approach can be implemented. All healthcare workers must realize that the prevention and control of HCAI is everyone's responsibility. However, this must be accompanied by suitable educational programmes. Brady *et al.* found that over two-thirds of surgical trainees in the UK were unaware of policies for the transfer of MRSA-positive patients, and 62% were

misinformed about the prevalence of MRSA bloodstream infections [27]. This implies that, apart from an educational deficit, there may remain a perception that the prevention and control of infection is largely the responsibility of specialist personnel, whose responsibility it is to minimize all infections, including those caused by MRSA.

The successful implementation of healthcare bundles to reduce central line-associated infections [28] suggests that it is possible to reduce HCAs, including MRSA infections, to an irreducible minimum, but this requires a major change in attitude. However, such a change will result in improvements in the quality and safety of patient care, and is likely to have significant cost benefits for the health services and society. In conclusion, guidelines for the prevention and control of MRSA are effective if they are implemented and if they are resourced. In many European countries, this requires a major change in culture, so that the quality and safety of patient care are prioritized.

Transparency Declaration

H. Humphreys is in receipt of research funding from 3M, Steris Corporation, Inova8 Technologies Ltd, and Pfizer. He has also recently received lecture and or consultancy fees from 3M and Astellas.

References

1. Vincent J-L, Sakr Y, Sprung CL *et al.* Sepsis in European intensive care units: results of the SOAP study. *Crit Care Med* 2006; 34: 344–353.
2. Cosgrove SE, Sakoulas G, Perencevich EN, Schwaber MJ, Karchmer AW, Carmeli Y. Comparison of mortality associated with methicillin-resistant and methicillin-susceptible *Staphylococcus aureus* bacteraemia: a meta analysis. *Clin Infect Dis* 2003; 36: 53–59.
3. De Vos J-Y, Elseviers M, Harrington M *et al.* Infection control practice across Europe: results of the EPD. *EDTNA/ERCA J* 2006; 33: 38–41.
4. Humphreys H. National guidelines for the control and prevention of methicillin-resistant *Staphylococcus aureus*—what do they tell us? *Clin Microbiol Infect* 2007; 13: 846–853.
5. Humphreys H. Implementing guidelines for the control and prevention of methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant enterococci: how valid are international comparisons of success? *J Hosp Infect* 2006; 62: 133–135.
6. MacKenzie FM, Bruce J, Struelens MJ *et al.* Antimicrobial drug use and infection control practices associated with the prevalence of methicillin-resistant *Staphylococcus aureus* in European hospitals. *Clin Microbiol Infect* 2007; 13: 269–276.
7. Loveday HP, Pellowe CM, Jones SRLJ, Pratt RJ. A systematic review of the evidence for interventions for the prevention and control of methicillin-resistant *Staphylococcus aureus* (1996–2004): report to the joint MRSA Working Party (Subgroup A). *J Hosp Infect* 2006; 63S: S45–S70.
8. Cooper BS, Stone SP, Kibbler CC *et al.* Systematic review of isolation policies in the hospital management of methicillin resistant *Staphylococcus aureus*: a review of the literature with epidemiological and economic modelling. *Health Technol Assess* 2003; 7: 1–194.
9. Stone SP, Cooper BS, Kibbler CC *et al.* The ORION statement: guidelines for transparent reporting of outbreak reports and intervention studies of nosocomial infection. *J Antimicrob Chemother* 2007; 59: 833–840.
10. Kendall JB, Hart CA, Pennefather SH, Russell GN. Infection control measures for adult cardiac surgery in the UK—a survey of current practice. *J Hosp Infect* 2003; 54: 174–178.
11. Report of a combined working party of the British Society for Antimicrobial Chemotherapy, the Hospital Infection Society and the Infection Control Nurses Association. Revised guidelines for the control of methicillin-resistant *Staphylococcus aureus* infection in hospitals. *J Hosp Infect* 1998; 39: 253–290.
12. Fitzpatrick F, Roche F, Cunney R, Humphreys H. Strategy for the Control of Antimicrobial Resistance in Ireland Infection Control Committee. Challenges of implementing national guidelines for the control and prevention of methicillin-resistant *Staphylococcus aureus* colonization or infection in acute care hospitals in the Republic of Ireland. *Infect Control Hosp Epidemiol* 2009; 30: 277–281.
13. Schelenz S, Tucker D, George C *et al.* Significant reduction of endemic MRSA acquisition and infection in cardiothoracic patients by means of an enhanced targeted infection control programme. *J Hosp Infect* 2005; 60: 104–110.
14. Hails J, Kwaku F, Wilson AP, Bellingan G, Singer M. Large variation in MRSA policies, procedures and prevalence in English intensive care units: a questionnaire analysis. *Int Care Med* 2003; 29: 481–483.
15. Cepeda JA, Whitehouse T, Cooper B *et al.* Isolation of patients in single rooms or cohorts to reduce spread of MRSA in intensive-care units: prospective two-centre study. *Lancet* 2005; 365: 295–304.
16. Huskins WC, Goldmann DA. Controlling methicillin-resistant *Staphylococcus aureus* aka ‘Superbug’. *Lancet* 2005; 365: 273–275.
17. Wertheim HFL, Vos MC, Boelens HAM *et al.* Low prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA) at hospital admission in the Netherlands: the value of search and destroy and restrictive antibiotic use. *J Hosp Infect* 2004; 56: 321–325.
18. van Trijp MJCA, Melles DC, Hendriks WDH, Parlevliet GA, Gommans M, Ott A. Successful control of widespread methicillin-resistant *Staphylococcus aureus* colonisation and infection in a large teaching hospital in The Netherlands. *Infect Control Hosp Epidemiol* 2007; 28: 970–975.
19. Vriens M, Blok H, Fluit A, Troelstra A, van der Werken C, Verhoef J. Costs associated with a strict policy to eradicate methicillin-resistant *Staphylococcus aureus* in a Dutch university medical centre: a ten year survey. *Eur J Clin Microbiol Infect Dis* 2002; 21: 782–786.
20. Lucet J-C, Paoletti X, Lolom I *et al.* Successful long-term programme for controlling methicillin-resistant *Staphylococcus aureus* in intensive care units. *Int Care Med* 2005; 31: 1051–1057.
21. Harrington G, Watson K, Bailey M *et al.* Reduction in hospital wide incidence of infection or colonisation with methicillin-resistant *Staphylococcus aureus* with use of antimicrobial hand-hygiene gel and statistical process control charts. *Infect Control Hosp Epidemiol* 2007; 28: 837–844.
22. Huang SS, Yokoe DS, Hinrichsen VL *et al.* Impact of routine intensive care unit surveillance cultures and resultant barrier precautions on hospital-wide methicillin-resistant *Staphylococcus aureus* bacteremia. *Clin Infect Dis* 2006; 43: 971–978.
23. Clancy M, Graepler A, Wilson M, Douglas I, Johnson J, Price CS. Active screening in high-risk units is an effective and cost-avoidant method to reduce the rate of methicillin-resistant *Staphylococcus aureus* infection in the hospital. *Infect Control Hosp Epidemiol* 2006; 27: 1009–1017.

24. Gerber SI, Jones RC, Scott MV *et al.* Management of outbreaks of methicillin-resistant *Staphylococcus aureus* infection in the neonatal intensive care unit: a consensus statement. *Infect Control Hosp Epidemiol* 2006; 27: 139–145.
25. Ofner-Agostini M, Varia M, Johnston L *et al.* Infection control and antimicrobial restriction practices for antimicrobial-resistant organisms in Canadian tertiary care hospitals. *Am J Infect Control* 2007; 35: 563–568.
26. Nathwani D, Morgan M, Masterson RG *et al.* Guidelines for UK practice for the diagnosis and management of methicillin-resistant *Staphylococcus aureus* (MRSA) infections presenting in the community. *J Antimicrob Chemother* 2008; 61: 976–994.
27. Brady RR, McDermott C, Gibb AP, Paterson-Brown S. Fact or fiction; do surgical trainees know enough about infection control? *Ann R Coll Surg Engl* 2008; 90: 647–650.
28. Pronovost P, Needham D, Berenholtz S *et al.* An intervention to decrease catheter-related bloodstream infections in the ICU. *N Engl J Med* 2006; 355: 2725–2732.